AMERICAN JOURNAL OF PHARMACY

and

THE SCIENCES SUPPORTING PUBLIC HEALTH

SINCE 1825

JOSEPH ROSIN

Scientist, Editor (see page 2)

JANUARY
1941

Ref.

PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE

Announces New Popular Science Lectures

Following a custom established twenty years ago, the Philadelphia College of Pharmacy and Science announces a series of Popular Science Talks for the 1941 Season. These lectures, delivered by members of the faculty of this, the oldest institution of its type in the Americas, are designed especially to combine scientific accuracy and completeness with a minimum of technical terms.

The general public, especially high school students and others interested in the sciences of the world today, are cordially invited to attend as many of these Wednesday evening talks as they wish, and to bring their friends with them. There are no cards of admission, the doors being open to all who are desirous of spending profitable hours in the realm of the marvels of modern science.

The first of the current series of talks will be delivered on Wednesday, February 12, 1941. Other lectures will follow each Wednesday night for ten weeks. Each commences promptly at 8.30 P. M., and lasts for about an hour. Wherever possible, experiments, motion pictures, lantern slides and exhibits will be used to illustrate the diverse subjects.

Following is the list of lectures and lecturers:

February 12—"Kitchen Science", by Professor Freeman P. Stroup.

February 19—"Textiles from Test-tubes", by Dr. Ivor Griffith.

February 26—"An Ounce of Prevention", by Professor L. F. Tice.

March 5—"The Sulfa-Miracle Drugs", by Dr. Louis Gershenfeld.

March 12—"Foods—Their Adulteration and Misbranding", by Dr. J. W. E. Harrisson.

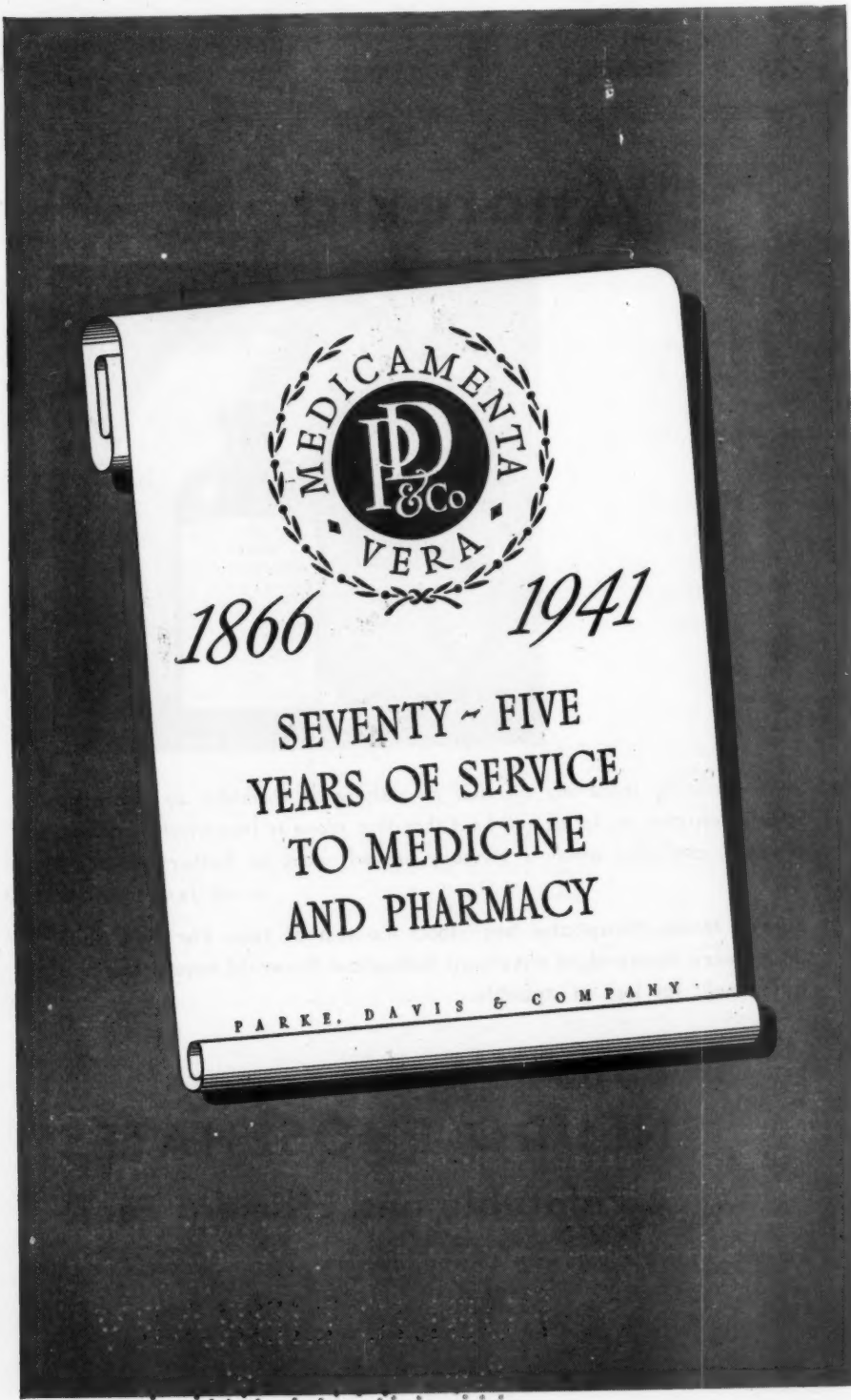
March 19—"Television", by Dr. George Rosengarten.

March 26—"Radioactivity—Natural and Artificial", by Dr. Donald P. LeGalley.

April 2—"Plant Blood—The Story of Chlorophyll", by Prof. E. H. MacLaughlin.

April 9—"Your Good Health is Good National Defense", by Mr. John E. Kramer.

April 16—" 'Vita' Means Life", by Dr. John N. McDonnell.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JOSEPH ROSIN

THE journal has placed upon its cover the picture of Joseph Rosin. Few pharmacists are familiar with the extensive contributions to medicinal standards that he has made. Although born in Russia, his college training was received at the University of Pennsylvania, where he graduated in 1909 with the Bachelor of Science degree. In 1925 the Philadelphia College of Pharmacy and Science bestowed upon him the honorary degree of Master of Pharmacy.

From 1913 to 1927 he was chief chemist for the Powers-Weightman-Rosengarten Company and, in 1927, became vice-president and chemical and research director of Merck and Company.

He is a member of the Committee on Analytical Reagents of the American Chemical Society, and he holds membership in the American Association for the Advancement of Science, the American Institute of Chemists, the American Institute of Chemical Engineering, the American Pharmaceutical Association and the London Chemical Society. Since 1910 he has rendered invaluable assistance in the preparation of the chemical standards for both the United States Pharmacopœia and the National Formulary and has written the texts for practically all of the U. S. P. reagents.

In 1937 he published "Reagent Chemicals and Standards," a 500-page volume recognized as the authority for reagent standards in the United States. He is also editor of the well-known reference "Merck Index."

Since 1936 he has been a member of the Board of Trustees of the Philadelphia College of Pharmacy and Science.

E D I T O R I A L

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful. The editor, alone, is responsible for their type, their tone and their tenor.

RADIO — ACTIVITY

SOMETIME ago, in an editorial entitled "The Rape of the Radio," it was hopefully predicted that the authorities would be so vested with new weapons by virtue of the recent Food, Drug and Cosmetics Act, that blatant patent medicines with impossible and vulgar claims would soon pass into a well-merited oblivion. As yet, that prediction has not come true, although there are portents of progress.

We now reprint part of the above-mentioned editorial because of its pertinence and impertinence in view of the Federal Trade Commission's complaint noted later in this bit of writing. Here it is,—

"But there is neither curb nor law to regulate the radio. For proper pay anyone may use—or anyone abuse it. And that which is worth-while on the ether is ruined by its contemptible company.

"Quackeries, too rank to find a place in public print, godiva through the air with a crudeness and a rudeness unashamed.

"From New York—directly from the editorial offices of the Journal of Living (sic!) comes a jerky voiced crusader waging a strictly impersonal (!) fight for catharsis. Gobs of staccato-stuff are spilled on the ether—by the editor himself—who is the avowed enemy of the 'blasting, corroding, dynamite dissemblers of the 30 feet of the delicate membrane called guts'—and who is the friend—*disinterested* friend 'passionately and devoutly positive of the value'—of a product which he calls SERUTAN—and which absolutely corrects 'food delay'; and all the diseases, maladjustments, disasters, inconveniences, despairs and discomforts appertaining thereto! Says he, 'Slim yourself with Serutan!'

"He is as voluble as a victrola, as suave as sleet and as accurate as an almanac—but he is as deadly certain as death itself.

"And there are thousands who do listen to this self-labelled expert, who answers all queries in all fields of medicine, and whose meager-minded ministry cannot help but do damage.

"But he *does* sell SERUTAN—else his broadcasting would long since have ceased!" (Unquote!!!)

And now read this:

Recently the Federal Trade Commission issued a complaint against the promoters of Serutan, the latter now extensively advertised as a remedy for constipation.

The complaint charged the representation:

> "That Serutan has substantial therapeutic value in restoring and maintaining natural elimination, that it stimulates and strengthens and promotes normal and regular action on the part of the digestive and eliminative organs and muscles, and
>
> "That it constitutes a cure or remedy for and possesses substantial therapeutic value in the treatment of constipation."

The complaint alleged:

> "That Serutan has no therapeutic value with respect to restoring or maintaining natural elimination.
>
> "That it is not capable of accomplishing the results claimed.
>
> "That it possesses no therapeutic value in the treatment of constipation except insofar as its laxative properties may assist in the temporary evacuation of the intestinal tract.
>
> "That the active ingredient of the preparation consists of the mucilaginous portion of psyllium seed, and
>
> "That the presence of this ingredient serves to give the preparation the properties of a mild laxative 'aside from which properties the product is wholly without therapeutic value.'"

Mind you, every city of any size in America scatters into the ether from its transmitting stations gobs and gobs of nonsense quite as ludicrous as this Serutan silliness.

For instance, if you dial a Philadelphia station—licensed to a great store that prides itself upon the quality of its merchandise and the purity of its food, you may listen in—as thousands do—you may listen to the Voice of Health—and so postpone your funeral!

A marmalady voice—obviously spread to cover the crust—comes slowly and funereally, like the sound of a great amen—seeping unwillingly through a reluctant ether. But when it does come, it comes not as a viscid jell, in thuds or gobs, but like a gentle, blood warm unguent teasing the ear drums to let a passage through.

Listen! "Would you have your blood vessels whitewashed inside?" or "would you rather keep them young, tensile and elastic?"

"Do you want to spend your old age harkening to the tune of cracking arteries?"

For youth's sake—says the basso profundo—for pity's sake—(and especially for *my* pocketbook's sake, which he does *not* say) take Mar-min and keep your alkaline balance. Mar-min, by the way, is an essence of sea-vegetables containing 200 times as much iron as liver (!), 1000 times as much iodine as fish (poor fish)—yet Mar-min is *not* a medicine—but a food!

O Tempora! O Mores!!

It may be that in due course, and perhaps when our national defense program is well under way, we shall find the Federal Trade Commission catching up to such trespassings on truth and travesties on good taste.

One finds it still difficult to spend a radio-active hour without being annoyed with such pathologic stuff as "boons to women," "community catharsis," "coughs resulting from colds," et al., *ad nauseam.*

But for the moment we confess that the greatest joy of the radio is its convenient turnitoffness!!

IVOR GRIFFITH.

THE CONTROL OF CANCER

ALL over our country today there is a new spirit of determination and resolution. We have watched overseas the clash of a cruel and coldly impersonal type of social order with the less efficient but far more human organization called Democracy. From the very outset we knew in our hearts which was right and which was wrong. Because of the very kindness and consideration on which our sort of Civilization was founded we were at first unable to grasp the full menace of the forces arrayed against it. Now, however, we are awake, alert and active. We have taken up our position and we cannot relinquish it until final and complete victory. What a close parallel there is between this situation and that of the problem of cancer control.

For decades we have known that cancer was a cruel and ruthless killer, an enemy of homes and of human happiness. It has taken men and women in their prime—leaders in art, in science, and in industry. It has broken up families and robbed children of their parents. For years it has been a menace while we allowed it to breed fear and discouragement.

Because other diseases were less vigorous and menacing, and because they provided us with less opposition in diagnosis and treatment, we have attacked them first and with more optimism. One after another they have been checked or beaten. Now, however, we are finally aroused as a people and have taken our stand as regards cancer. No longer can it be allowed to move unchecked and terrible. We know that it is vulnerable. It is no mystical being that can defy the assault of knowledge and science activated by courage and idealism. Some with special training knew this for some time, however, before it was possible to enlist and use the will of the general public in the fight. What has made the difference? Why can we today move forward with faith and hope?

It is the women of America who have made this possible. Rising as volunteers to participate in the organization of the Women's Field Army Against Cancer (a part of the work of the American Society for the Control of Cancer) they have done wonders. They have spread knowledge of the signs and symptoms that may mean cancer. Millions upon millions of people have received this information without cost. They have organized meetings which have been addressed by selected medical speakers. Under proper medical supervision, they have aided indigent patients to obtain diagnosis and treatment. They have removed the paralyzing fear of cancer that held the country powerless; they have transformed the whole battlefront against cancer from one where isolated raids were being made to a general and inspiring advance. They have brought courage and peace to thousands. They have begun to cheat Death of his prey.

This is good training for any sort of struggle, a type of preparedness for organized effort against tremendous evil. It is the logical and reasonable school for those qualities that Democracy must develop in order to survive. *That is why it is not only your duty but your privilege to take part in the fight against cancer.* To shirk that task is a poor prospect for your ability to meet the sort of challenge that Life will force upon all of us in the immediate future. To meet the call cheerfully and intelligently will help you to win other battles to come. The need is clear. Humanity calls. Enlist and Serve!

CLARENCE C. LITTLE, SC. D.
Managing Director, American Society for the Control of Cancer.

CORRESPONDENCE

The Pharmaceutical Society of Great Britain

17, Bloomsbury Square, London, W. C. I.

November, 1940.

Dear Fellow-Member:

Our Society has had nearly one hundred years of activity, full of ups and downs, but its members have never had such an anxious time as today, hence this personal appeal.

It is on behalf of pharmacists in different parts of the country whose pharmacies are in ruins; on behalf of those carrying on, but under notice from the military authorities to pack and leave at any time; on behalf of managers and assistants and hospital pharmacists of long service with no work and some with no home.

Their burden must be shouldered by all of us in pharmacy and the Society has opened a War-Aid Fund to help them.

From this fund pharmacists and students hit by the war will be given aid generously, having regard to any help given or available from other sources. It may provide money to salvage furniture, fees to keep children at school, rent while a new start is made, clothes and other necessities.

Will you give what you can, remembering that this is an emergency calling upon you to be open-handed and very ready and generous in your giving.

We will acknowledge your gifts from the Benevolent Fund, but earmark them for War Aid.

Yours sincerely,

WALTER DEACON,
President.

Editor's Note: The above appeal is for assistance to a worthy cause. This Journal will be glad to accept and transmit any contributions to the President of the Pharmaceutical Society of Great Britain.

The Revision Committee of the United States Pharmacopœia invites your consideration and criticism of the new articles recommended for admission to the U. S. P. XII (see page 17), and the U. S. P. XI articles to be deleted from the U. S. P. XII (see page 28).

GENERAL OBSERVATIONS ON THE U. S. P. STANDARDS AND TESTS*

By Joseph Rosin

SOME years ago the question was propounded why revise the monographs of U. S. P. preparations since, at the time these preparations were officialized, the standards drawn up for them must have been entirely satisfactory. The same question could be asked now. The answer to this question is quite simple. It is that which signifies advancement, betterment and refinement—"progress." Progress in medicinal products demands improvement of quality and refinement of processes, tests, and assays.

Purity of U. S. P. Products: Because of the advances and improvements in the quality that is continually being made by manufacturers of U. S. P. products, the U. S. P. has found it possible to raise the standards of quality in each succeeding revision, and due to the advances that have been made during the past decade, I believe that standards of several U. S. P. products can be further raised.

The quality of the mineral acids—hydrochloric, nitric and sulfuric —now marketed for Pharmacopœial uses closely approaches that of the reagent grade. The U. S. P. standard for Chromium Trioxide is not less than 95 per cent. Specifications for Chromium Trioxide used for chrome plating require not less than 99 per cent. CrO_3, so it would seem that the U. S. P. could well raise the assay minimum to that of the industrial grade. The permissible limit for lead in citric acid in U. S. P. X was 20 parts per million. In the U. S. P. XI this limit was halved to 10 parts. The quality of this acid now available justifies again halving the limit for lead. The per cent. purity of this acid can also be raised from 99.5 to 99.8 per cent.

Heavy Metals: The present U. S. P. general test for heavy metals permits approximately from 100 to 150 parts per million as lead. With very few exceptions the heavy metal content in U. S. P. chemicals now on the market is very much less. It is accordingly recommended that the limit and test for heavy metals be modified in this direction and preferably adopt a quantitative limit for heavy metals.

* Presented at the Pre-Convention Conference of the United States Pharmacopœia, Washington, D. C., and published in the *Oil, Paint & Drug Reporter.*

Solubilities: In the solubility paragraph the U. S. P. frequently includes a wide range of solvents. Whether or not solubilities in solvents which are not used in making pharmaceutic preparations of the chemical should be given, is a question on which the users of the Pharmacopœia may differ. There can be, however, no difference of opinion that whenever a definite figure for solubility is given it should be reasonably correct.

Notwithstanding the statement made in the General Notices that the solubility statements are not intended as physical constants but are primarily given as information, many laboratories apply the solubility data given in the U. S. P. as a test for quality. This has resulted in the discovery that some of the solubilities given in the U. S. P., particularly with ether as the solvent, are either incorrect or unattainable by the practical method of testing for solubility, i. e. adding the specified volume of solvent to the substance and shaking. As an example, the Pharmacopœia gives the solubility of quinine in ether as 1 gm. in 1.9 cc. In actual practice it requires many times this volume of solvent to dissolve 1 gm. of Quinine. This would indicate that the solubilities in ether or similar solvents should be redetermined in a manner that would be used in actual practice as just indicated above. The solubility in ether is particularly stressed here because ether may be of a variable composition, but we have also found solubilities in alcohol which did not conform to those given by authorities.

Melting Points: The apparatus for the determination of the melting point as prescribed in the present Pharmacopœia is not suitable and very inconvenient for use in laboratories where several melting points have to be made daily. I refer particularly to the method of stirring the bath by hand, heating by Bunsen burner, and regulation of the rate of heating to 3 degrees per minute for the last 20 degrees. In this mechanical electric age it is like going against the current to prescribe "hand-driven" machinery and Bunsen burners for heating. When the melting point is high, the regulation of the rate of heating to 3 degrees per minute for the last 20 degrees is difficult to attain. At the same time it would not seem advisable for the Pharmacopœia to prescribe an apparatus which would exclude the use of a simple

---

Progress in manufacturing technic leading to greater purity of chemicals is considered as a logical reason for the recognition of more exacting specifications for U. S. P. substances. The author also as a result of considerable experience in the application of U. S. P. tests recommends certain desirable modifications.

apparatus as, for instance, a hand-stirred one, or heating by Bunsen burner. To correct this situation it is my recommendation that the U. S. P. have reference melting point materials, about 5 or 6, covering the melting range from about 80 to 240 degrees; the correct melting point of these substances to be determined by several laboratories by the use of apparatus and a procedure to be described in the Pharmacopœia, but permission should be given to use any other apparatus or procedure capable of giving the proper melting point with the reference samples.

Polariscopic Tests: The measurement of the specific rotation should be extended to as many of the optically active U. S. P. products as practical. This determination is particularly indicated in cases where the melting point or specific tests for identity and purity are either absent or not entirely satisfactory. In this connection may be mentioned ethyl morphine hydrochloride, colchicine, cinchonidine and cinchonine sulfate (the latter two being official in the N. F.).

Determination of Ash: For this test the U. S. P. directs to "use as low a temperature as possible to effect the combustion of the carbon." The reason for using a low temperature is to prevent the volatilization of inorganic salts which may volatilize if higher temperatures are used. The combustion of the carbon, however, at a low temperature is rather tedious and time consuming. In cases where the carbon "fuses" it is indeed very difficult to burn it off at a low temperature. To obviate this difficulty I recommend that the ash be "sulfated." This is done by adding 0.5 cc. to 1 cc. of sulfuric acid to the quantity of the sample taken for the ash test, either before or after charring, and the material then ignited until free of carbon. With this procedure a relatively high temperature can be used without fear of volatilization of inorganic salts. This is especially desirable in the ashing of organics containing halogens. Furthermore, the sulfuric acid facilitates the combustion of the carbon. This procedure is already used in the Pharmacopœia in the determination of non-volatile in ammonium halides, the object of the sulfuric acid there being to arrest volatilization of alkali halides.

Assays: The quantities designated to be taken for the assays were not just taken at random but for definite reasons. In many of the assays, and especially in those involving back titrations, the quantity directed to be used must be fairly closely adhered to, otherwise the reaction may be incomplete or different than intended. Since,

however, the U. S. P. indicates the quantity to be used by "about," quantities of 25 per cent. less or greater than the quantity indicated are frequently weighed out for the assay, resulting in considerable discrepancies. To eliminate this source of inaccuracy, it is recommended that instead of saying, "weigh accurately *about* X Gm." it should be made to read: "weigh accurately from X to Y Gm."—the range to be made, let us say, 10 per cent. either way, for instance, if 0.2 Gm. is to be used, it should be given as "from 0.18 to 0.22 Gm."

Milligrams v. Grams: The use of ciphers preceding the significant figure in the statement of the weights to be used in the tests or assays is awkward in pronouncing, and in writing it frequently leads to errors, a cipher being added or omitted. Since the wide advance of the use of "micrograms" in chemical, biological, etc. work, the milligram has become a well-known unit of weight—as much practically as the gram. It is recommended, therefore, that when the quantity to be used for a test or assay is less than 0.1 gram, the U. S. P. give it in terms of milligrams. I would even prefer to go further and use milligrams for any fraction of a gram.

Identity Tests for Assay Products of Tinctures, Extracts, etc.: Although this has been proposed, I believe, for the former revision (U. S. P. XI) and has not been acted upon, perhaps for a good reason, I, nevertheless, again recommend that consideration be given in the forthcoming revision of the Pharmacopœia to include suitable tests for the identification of the assay product of U. S. P. galenicals, provided, of course, suitable identity tests are available.

The Nation Takes Its Medicines. *American Professional Pharmacist 6, 767* (1940). According to the latest figures released by the United States Bureau of Census, prescription drugs and medicines showed an increase of thirty-six million dollars for 1939 over 1937 and patent and proprietary medicines for public sale decreased eighteen million dollars in value in the same period. The actual value of prescription medicines in 1939 was $178,930,487. The value of "over the counter" medicines in that year was $166,577,263.

J. E. K.

PHYSICAL PROPERTIES AS A BASIS FOR THE IDENTIFICATION OF SOLID STUFFS*

By C. J. Campbell

The identification of medicinal substances based on purely chemical considerations is not only time consuming, but it requires the attention of a skilled chemist. Physical determinations centered largely around the polarizing microscope may easily shorten and simplify many such identifications.

THE difficulties involved in the identification of stuffs of complicated molecular structure by chemical means are, we believe, generally conceded. Relatively simple materials may present serious difficulties if there are several possible stuffs containing identical radicals or having the same empirical formula. The problem becomes immeasurably more difficult if the examiner has not a thorough chemical training. The possibility of making such identifications on the basis of properties belonging to the molecule as a whole using the methods of the petrographer has long been recognized (1) (2) (3) (4) (5) (6) (7). The available methods are described in numerous publications (8) (9) (10) (11) (12) (13).

In teaching medical students we have observed that the simpler chemical procedures outlined in the usual manuals of laboratory work in toxicology or pharmacology are often ambiguous and in many instances depend on the recognition of qualities for which there is no simple exact language. Because of the difficulties and ambiguities in established chemical methods and because most medical students are not trained chemists, it has seemed advisable to find methods which were relatively simple, the results of which could be expressed numerically or in unambiguous symbols. A complete microscopic, crystallographic examination requires too elaborate equipment and too specialized skills. However, it is, we believe, unnecessary to go to such refinements of technique if one is willing to add to the simpler mineralogical methods other objective determinations which are not too complicated. The methods which we have adopted follow.

Preliminary Microscopic Examination

Representative fragments immersed in some suitable liquid (usually one of the oily stuffs used in determining refractive indices) in which they are insoluble are examined under the microscope. This ordinarily shows immediately if the unknown material is organized,

*Presented at the Pre-Convention Conference of the United States Pharmacopœia, Washington, D. C.

unorganized, homogeneous or a mixture. If organized, the identification is attempted on the basis of the cell structure. If unorganized and a mixture, the component parts, if possible, are separated, usually by differences in solubility. Given a single unorganized substance, one proceeds by determining first a melting point.

Melting Point Determinations

These have been undertaken by various methods and in general it has been found that the smaller the amount of material used the less was the guesswork as to just when melting took place. We have come to attempt the determination on a single crystal or fragment of a crystal. This, of course, involves the use of the microscope. Cf. (11) vol. 1, p. 209. One of our students, J. C. Lilly, dissatisfied with the methods available in this laboratory is now working on a modification of an apparatus described by Ray and Dagal (14) which gives promise of affording the most clean-cut end points for melting point, transition points, sublimation point, decomposition point and freezing point that we have yet seen.

Tables of properties according to melting points are readily available for many stuffs in the International Critical Tables (15) and in the Handbook of Chemistry and Physics (16).

Fluorescence

The powdered material or a solution of it is placed in a dark box where it is exposed to radiation from a small ultra violet source (argon-filled glow lamp or small steri-lamp) passed through a "black glass" filter. The presence or absence of fluorescence is noted. An estimate of the color and intensity of fluorescence, if striking, is noted. Information on methods, a bibliography, and tables of results are to be found in Radley and Grant's Fluorescence Analysis (17).

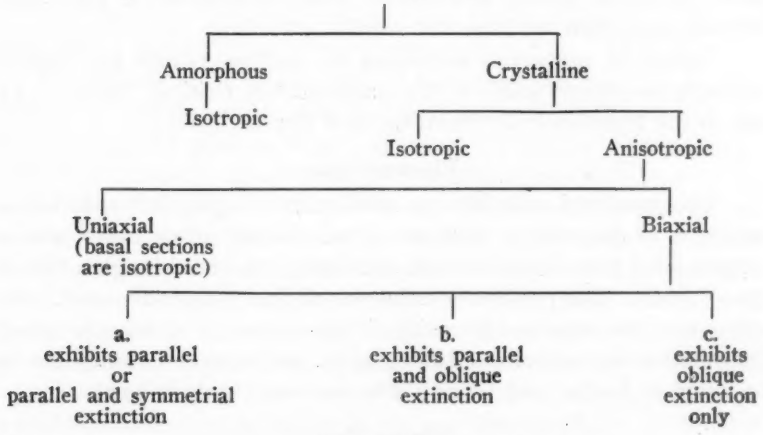
Flame Test

A small amount of the unknown material is placed on a clean nichrome loop and placed in a non-luminous flame. An indication of the character of the material is furnished by the combustion. Charring is taken as an indication that the stuff is organic. A colored flame without charring indicates a probable inorganic stuff and makes it worth while examining the emission spectrum with a small spectroscope having an included wave length scale. Spectrographic determinations are considered too elaborate to fall within the scope of the present scheme.

With the information obtained by the above methods the examination necessary with the polarizing microscope is considered to be much simplified. Any microscope having a rotatable stage and a polarizer and analyzer (these may be polaroid) will serve. A slot for the insertion of a first order red plate is an added convenience. A "chemical microscope" is more than adequate and a petrographic microscope, though it speeds the examination considerably, is not necessary.

Microscopic Examination

Notes are taken on the color and shape of the particles or crystals, keeping in mind always that the shape of ground fragments is probably not significant although such fragments are just as useful as perfectly formed crystals for many determinations. The material is then examined between crossed nicols and within the course of a minute one should be able to classify the material as



Cf. (11) vol. 1, pp. 270 et seq. and (13) pp. 147 et seq.

The remainder of the examination, if the stuff is amorphous, is simple. It will have but a single refractive index. This is determined by the immersion method (8) (9) (11) (13). A critical examination of refractive index determinations is given by Saylor (18).

The solubilities of the material in at least four different solvents, e. g. water, alcohol, ether, chloroform, are then determined. In these measurements we have been content to label the solubilities as insoluble, slightly soluble, soluble and very soluble. Estimates of the degree of solubility are readily made with the microscope. Into a

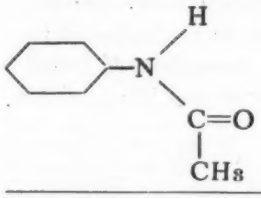
small drop of the solvent placed on a slide is pushed a fragment of the material being examined. (Very volatile solvents may have to be protected by a cover glass roof elevated on one edge by a fragment of very slender glass rod.) If the contours of the fragment are unchanged, the stuff is considered insoluble. If corners are rounded, it is considered slightly soluble. If the material appears to melt slowly, it is considered soluble. If the stuff appears to vanish rapidly surrounded by zones of "schlieren," it is considered very soluble.

Materials which are crystalline but isotropic, having only one index of refraction, are treated exactly as are the amorphous stuffs. On uniaxial crystals two indices are determined and on biaxial crystals three if possible. Suitable liquids for immersion are discussed in (8) (9) (11) (13) and (18).

The solubility determinations are of course identical in all classes.

A form which is used in the routine examination of unknown materials is given below as filled out for a known substance. The properties marked * are not considered essential in the analysis and have not been discussed. Those marked † may be determined incidentally in the analysis outlined.

ACETANILID



Group II A

M.P. 114.2 (Int. Crit. Tables Sublimes)
B.P. 303.8

sl. sol	HOH	sol ROR
v sol	ROH	sol $CHCl_3$

System † Orthorhombic
Cleavage *
Habit † rods, thin plates
N 1.506, 1.516, 1.627 all ± 0.001
Extinction II
Pol. colors † dull
Doub. refract *
Elongation † +
Class biaxial
Int. figs. * frequent
Opt. angle *
Opt. sign * —
Dispersion *

Fluorescence, doubtful blue
Flame, burns, sooty flame

The Pharmacopœial description of Acetanilid might thus be altered to run:

Description and Physical Properties—Colorless, shiny crystals, anisotropic, biaxial, exhibiting parallel extinction; the refractive indices are 1.506, 1.516 and 1.627, all ± 0.001. Melting point 113 degrees to 115 degrees C. "One gram of acetanilid is soluble in 190 cc. of water, etc. . . ." The additional information included in the above description adds, we believe, very materially to its definiteness.

One attempting to identify an unknown stuff can run through the entire scheme, excepting the refractive indices, in five minutes. The determinations of these latter may take from a few minutes to about half an hour. We feel sure that we accomplish analysis in fifteen minutes that would take days by chemical methods. So far there have been no failures or incorrect results. The total number is however too small to warrant statistical treatment.

Adequate complete tabulations of the various properties are to the best of our knowledge not yet available.

Summary

This is a report of the successful use of old recognized methods, centered about the polarizing microscope, by individuals who are definitely not crystallographers. The definiteness of the methods and the time-saving effected are stressed. The possible desirability of including in the Pharmacopœia the measurements listed and the need for more complete tabulations are mentioned.

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ARTICLES NOT OFFICIAL NOW BUT RECOMMENDED FOR INCLUSION IN U. S. P. XII

Absorbent Gauze
Absorbent Gauze, Sterile
Adhesive Absorbent Compress
Antipneumococcus Serum (the new monograph to cover all types)
Calaminae Preparata
Calcium Mandelate
Dextrose Solution (for injection 50 per cent.)
Dextrose (50 per cent.) and Sodium Chloride (30 per cent.) Solution (for injection)
Elixir Cardamomii Compositum
Elixir Iso-Alcoholicum
Elixir Phenobarbitali
Elixir Terpini Hydratis
Ethyl Carbamate
Gas-gangrene Antitoxin (to include types now used)
Gauze Bandage
Glycocoll (Amino Acetic Acid)
Immune Serum for Scarlet Fever, Human
Immune Serum for Measles, Human
Immune Globulin (Placenta Extract) Human
Lotio Calaminae
Lotio Calaminae Phenolata (2 per sent. Phenol)
Magnesium Trisilicate
Oleum Hippoglossi (Halibut)
Ouabain
Picrotoxin
Picrotoxin Solution (for injection)
Potassii Chloridum
Quinine Hydrochloride
Quinine Hydrochloride with Ethyl Carbamate Solution (for injection)
Riboflavin
Ringer's Solution
Serums, Dry and Liquid forms authorized for all U. S. P. Serums
Surgical Silk and other Surgical Sutures
Surgical Silk and other Surgical Sutures Sterilized
Syrupus Ammonii Mandelatis
Syrupus Glycyrrhizae
Syrupus Rubi Ideaei
Tabellae Aminopyrinae
Tetanus Toxoid
Tetrachloroethylene
Theobromine with Sodium
Totaquinine
Transfusion Normal Plasma, Human
Transfusion Normal Serum, Human
Trichloroethylene
Urea
Vitamin A and D in Oil (Cod Liver Oil Strength)
Zinc Peroxide

The following additional items, needed as "pharmaceutic necessities," must be added as new admissions—

Compound Spirit of Cardamon
Oil of Caraway
Oil of Cardamon
Raspberry Juice
Spirit of Bitter Almond
Tincture of Cudbear

AN IODATE ASSAY FOR RELATIVELY PURE ASCORBIC ACID

By William Bandaruk

IN THE course of a study of methods of assay for pharmacopœial quality ascorbic acid it occurred to the writer to investigate the possibility of employing potassium iodate volumetric solution as a quantitative oxidant for this substance, using essentially the same procedure as is prescribed in the United States Pharmacopœia for the assay of potassium iodide.

The proposed assay was carried out as follows: About 0.2 gram of ascorbic acid (Merck), previously dried overnight in a sulfuric acid desiccator and accurately weighed, was dissolved in 25 cc. of 6N hydrochloric acid in a glass-stoppered flask; to this was added 10 cc. of chloroform and the mixture titrated with M/40 potassium iodate to the disappearance of the purple color in the chloroform layer. The last portions of iodate solution were added dropwise, the mixture being agitated vigorously and continuously.

Assuming the following reaction to take place:

$$2C_6H_8O_6 + KIO_3 + 2HCl \longrightarrow 2C_6H_6O_6 + ICl + KCl + 3H_2O$$

each cc. of M/40 potassium iodate represents 0.008803 gram of ascorbic acid.

Results obtained by this method of assay and by the U. S. P. XI Second Supplement assay, which involves oxidation with N/10 iodine solution, are set forth in the following table.

Results of Assay of Ascorbic Acid

Sample (Grams)	Amount Found by Titration (Grams)	Per Cent. Ascorbic Acid
U. S. P. XI Second Supplement Assay Using N/10 Iodine		
0.2043	0.2048	100.2
.2054	.2058	100.2
.2287	.2093	91.5
.2818	.2593	92.0
.2665	.2552	95.8
.2169	.2171	100.1

Assay With M/40 Potassium Iodate

.2108	.2101	99.7
.2191	.2188	99.8
.2143	.2142	99.9
.2126	.2123	99.9
.2331	.2329	99.9
.2350	.2345	99.8
.2253	.2248	99.8
.2027	.2026	99.9
.2163	.2159	99.8
.2284	.2283	99.9

From a comparison of the results obtained by the two methods of titration it is apparent that the proposed iodate oxidation method is capable of greater precision than the official iodine oxidation procedure. In the latter, a difficulty was encountered in the fading of the end point. This experience was also reported to the writer by others who have used the pharmacopœial assay. In the iodate method no such problem arises and the results are much more consistent.

Summary

A method for the assay of relatively pure ascorbic acid, involving oxidation with potassium iodate volumetric solution, has been developed. Comparison of the results obtained by this method with those obtained by applying the U. S. P. XI Second Supplement iodine oxidation procedure indicates that the former is capable of greater precision than the official method.

Acknowledgment

The author wishes to acknowledge the advice and help extended him by Dr. Arthur Osol, Director of the Chemical Laboratories of the Philadelphia College of Pharmacy and Science.

PROPOSED CHANGES IN FORMULAS FOR U. S. P. TINCTURES OF IODINE*

By C. O. Ewing and L. S. Crosby

In preparing monographs for Tincture of Iodine and Mild Tincture of Iodine U. S. P. XI, certain trade practices concerned with the purchase of a specially denatured alcohol were overlooked. This has resulted in considerable difficulty to many manufacturers without any demonstrable improvement in the products themselves. A remedy for this present condition is suggested.

I. Tincture of Iodine U. S. P. XI—Second Supplement

WHILE the U. S. P. has an official procedure for making Tincture of Iodine, in actual practice it rarely is made that way because the finished commercial tincture made with specially denatured alcohol can be purchased more cheaply than the official raw materials alone can be secured through the usual channels of trade. These savings can be passed along to the public, which of course was the original intent of the government, when the use of denatured alcohol for industrial purposes was instituted several decades ago.

The specially denatured alcohol first authorized for use in making Tincture of Iodine was No. 25. It directed merely that 15 pounds of Potassium Iodide and 20 pounds of Iodine be dissolved in 100 gallons of Ethyl Alcohol.

It was found in actual practice that the denaturants were difficultly soluble in the alcohol, which resulted in material irreglarities in their concentrations in the alcohol as delivered to pharmaceutical manufacturers.

Accordingly, a supplementary formula was issued (1) as Specially Denatured Alcohol No. 25-A, which directed that "To every 100 gallons of Ethyl Alcohol add: a *solution* composed of 20 pounds of Iodine, U. S. P., 15 pounds of Potassium Iodide or Sodium Iodide, U. S. P., 15 pounds of water." This produces an alcohol in which the denaturants are completely soluble and which contains between 90 and 92 per cent. by volume of Ethyl Alcohol.

*This paper is based on two reports read at the Pre-Convention Conference of the United States Pharmacopœia.

The regulations also prescribe the formula for preparing U. S. P. Tincture Iodine which must be adhered to when using Specially Denatured Alcohol No. 25-A. This formula produces a finished tincture having an Ethyl Alcohol content of about 83 per cent. by volume.

The U. S. P. XI apparently took cognizance of this commercial practice and specified an alcohol content of "80 to 85 per cent. by volume." The second supplement to the U. S. P., however, changed the alcohol limits to "85 to 90 per cent.," possibly based upon a theoretical inspection of the formula as outlined in the Pharmacopœia. Inasmuch as the normal range of alcohol by volume in Specially Denatured Alcohol No. 25-A is 90 to 92 per cent., less water is available to prepare the solution of Iodine and Potassium Iodide than the regulations direct and good technique requires. This makes it very difficult, if not impossible, to prepare a finished tincture that complies with the new alcohol limits.

Inasmuch as this difference of a few per cent. of alcohol in the finished product has no bearing whatsoever on the therapeutic efficacy of the finished product, we feel that the Revision Commiittee should recognize the usual trade practice which benefits the ultimate consumer and revert to the previous standard of 80 to 85 per cent. alcohol by volume in U. S. P. Tincture of Iodine.

II. Mild Tincture of Iodine, U. S. P. XI

Mild Tincture of Iodine, U. S. P. XI, is the only official preparation of this general type in which Sodium Iodide rather than Potassium Iodide is used to facilitate solution of the iodine. Potassium Iodide is used in the full strength Tincture of Iodine, U. S. P., Compound Solution of Iodine, U. S. P., Stronger Tincture of Iodine, N. F., and Tincture of Iodides, N. F. There are a number of objections to the use of Sodium Iodide from a practical standpoint.

1. The previous section has pointed out the economic advantage to the medical profession and to the ultimate consumer of commercial manufacture of Iodine tinctures and solutions using specially denatured alcohols. The use of Sodium Iodide in Mild Tincture of Iodine requires a special denatured alcohol for this preparation only. This requires a special permit and the carrying of extra stocks of this one raw material with consequent extra cost of handling.

2. The expensive component of both salts is iodine and since Sodium Iodide contains 84.66 per cent. iodine, whereas Potassium Iodide contains only 76.45 per cent. Iodine, the former is more expensive. The current comparative costs are $2.30 and $1.35 per pound, respectively. The net result is that Specially Denatured Alcohol No. 25-A with Sodium Iodide costs about seven cents more per gallon than with Potassium Iodide. This objection applies to manufacture by the individual pharmacist as well, if he elects to make his own tincture.

3. Sodium Iodide is very deliquescent. The U. S. P. in fact permits the presence of up to 5 per cent. of water. This makes it more difficult to handle during storage and manufacture.

4. It has been our observation that unless the U. S. P. method of assay for Sodium Iodide is carried out meticulously there is a decided tendency to obtain high results. This is due to incomplete volatilization of iodate or substances other than the Sodium Iodide. For this reason the U. S. P. assay directs the addition of repeated quantities of distilled water and redrying *on a waterbath* until a white residue is obtained. It is noteworthy that on page 343 of the U. S. P. XI under "Sodium Iodide—in the directions for drying to constant weight a temperature of 120 degrees C. is prescribed—a temperature appreciably higher than reached on the water bath.

   Consequently, we have found that it is difficult to get the residue down to constant weight in following the U. S. P. method, and also that there is a strong tendency for the residue to pick up weight during the weighing operation, both of which make for high results. Because of these facts, we recommend that the Revision Committee give consideration to such an essentially minor change as substituting Potassium Iodide for Sodium Iodide in the formula for Mild Tincture of Iodine in the next revision of the U. S. P. We feel that no physician would object to the presence of potassium ion in Mild Tincture of Iodine any more than he does to its presence in Tincture of Iodine.

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THE STANDARDIZATION OF VITAMIN ASSAYS BY THE U. S. P.

By E. M. Nelson

THE first official action taken by the U. S. Pharmacopœia relating to vitamins concerned cod liver oil. The tenth Decennial Revision, which became official on January 1, 1926, carries the following language in the monograph on cod liver oil: "Cod liver oil may be assayed for its vitamin A potency and should then contain at least 50 units per gram. Cod liver oil so assayed must be labeled 'This unit is not a measure of the antirachitic activity of cod liver oil.'"

It is interesting to note that one of the tests for identity of cod liver oil which was first prescribed in U. S. P. VI, published in 1882 (I refer to the sulfuric acid test) was actually a test for the presence of vitamin A even though the existence of this substance was not recognized until thirty years later.

As knowledge increased concerning the vitamin content of cod liver oil and its value as an important source of vitamin D was realized, it became apparent that new standards for the vitamin content of cod liver oil were highly desirable. Accordingly, the chairman of the U. S. P. Revision Committee called a meeting of representatives of the industry and individuals engaged in vitamin research in various institutions on May 7, 1931. This and similar meetings have subsequently been referred to as meetings of the U. S. P. Vitamin Committee. There were twenty present at this meeting and communications were received from several others who had been invited to attend but were unable to be present. The principal topics of discussion were methods for the assays of vitamin A and D in cod liver oil, and suitable minimum standards for these vitamins in cod liver oil. The American Drug Manufacturers Association Committee on Vitamins had conducted extensive collaborative studies on the determination of vitamin A and D and the methods which they proposed formed a basis for a considerable part of the discussion. It was quite apparent that decisions had to be reached on many controversial questions before methods could be adopted or standards set, and the meeting served largely to outline the scope of problems to be solved. There appeared

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A contribution to the Pre-Convention Conference of the United States Pharmacopœia, this paper describes the development of the present U. S. P. Vitamin Advisory Board and points out the great service this body has rendered in bringing order to the standards for this tremendous industry.

to be unanimity of opinion with respect to the desirability of providing reference standards which could be used in vitamin A and D assays. Following the meeting, considerable correspondence ensued in which various proposals were made with respect to vitamin assays of cod liver oil and a second meeting of the U. S. P. Vitamin Committee was called for January 8, 1932.

The establishment of international standards and the definitions of units for four of the vitamins in June, 1931, at a conference on vitamin standardization sponsored by the Health Organization of the League of Nations, marks a definite milestone in the determination of vitamins. At this conference standards were adopted for vitamin A, B_1, C, and D and those standards, and subsequent standards adopted by the international conference, have been made available to all countries. Prior to that time vitamin units had been defined in terms of animal response under prescribed conditions. The international units were defined in terms of the biological activities of specified quantities of the prescribed standards. With the aid of the standards vitamin potency can be determined by comparing the response of animals fed a given quantity of the standard with the response of animals, under identical conditions of environment and fed the same basal ration, fed desired quantities of the unknown. This procedure eliminates in a large measure errors which were previously due to differences in animal response in different laboratories.

There were thirty present at the U. S. P. Vitamin Committee meeting held in New York on January 8, 1932. As the result of actions taken at this meeting, a new text for the monograph on cod liver oil was proposed which embodied minimum requirements for vitamin A and D potency and methods for the assay of these vitamins. It was prescribed that vitamin A and D potency be expressed in terms of international units. It was further recommended that there be provided for distribution to manufacturers of products having vitamin A or D potency a "Reference Cod Liver Oil" of known vitamin A and D potency, expressed in international units, to be used as a basis of comparison in vitamin assays. It was the hope of the committee that the Food and Drug Administration of the United States Department of Agriculture would be in a position to distribute in this country both the international vitamin standards and the reference cod liver oil, but this was found to be impractical. Consequently, the Pharmacopœia Vitamin Advisory Board was organized on June 27, 1932, with the approval of the U. S. P. Board of Trustees, for

the purpose of arranging for the preparation and distribution of vitamin standards within the United States, and also to advise on all matters pertaining to vitamin preparations recognized in the United States Pharmacopœia. This board consisted of Lafayette B. Mendel, H. C. Sherman, E. M. Nelson, E. F. Kelly and E. Fullerton Cook, chairman. The personnel of this board has remained the same except that, following the death of Dr. Mendel, E. V. McCollum was appointed as his successor.

On October 5, 1933, the Pharmacopœia announced the release of the U. S. P. Reference Cod Liver Oil which was to serve as a reference in the assay of vitamin A and vitamin D products. The Vitamin Advisory Board made arrangements for obtaining a lot of 60 gallons of suitable cod liver oil. This oil was obtained and destearinated under the supervision of the Bureau of Fisheries of the United States Department of Commerce. It was then put up in 30 cc. bottles and kept under refrigeration. The oil was assayed by methods which had been prescribed for the U. S. P. assay of cod liver oil by comparing its vitamin A and D potency with the international standards for these vitamins. Fifteen laboratories collaborated in these assays. A potency of 3000 U. S. P. units of vitamin A and 95 U. S. P. units of vitamin D was assigned to the oil on the basis of these assays. The U. S. P. units for these vitamins were defined as equivalent in biological value to the international units. Oil from this lot is the only oil which has been distributed up to this time by the Board of Trustees of the U. S. Pharmacopœial Convention under the name "U. S. P. Reference Cod Liver Oil." It was planned to assay this oil for both vitamins A and D at six-month intervals and, although this program has not been strictly adhered to, a sufficient number of assays have been made to show that there has been no demonstrable change in the potency of this oil since the time it was prepared. The planning of these assays and review of the results obtained has been assigned to the Vitamin Advisory Board.

On November 28, 1933, there was released to the U. S. Pharmacopœia Vitamin Committee an announcement of proposed standards for vitamins A and D in U. S. P. cod liver oil recommended by the Vitamin Advisory Board. The minimum standard for vitamin A was 600 U. S. P. units per gram and for vitamin D 85 U. S. P. units per gram. On the following day the chairman of the U. S. Pharmacopœia Revision Committee announced proposed methods for the assay of vitamin A and D in cod liver oil to be incorporated in an interim

revision of the Pharmacopœia. These methods had been prepared by the Vitamin Advisory Board on the basis of recommendations made by the U. S. Pharmacopœia Vitamin Committee.

On May 1, 1934, the chairman of the Revision Committee issued "U. S. Pharmacopœia X interim Revision Announçement No. 2, a 1934 Revision of the Text and Assays for Cod Liver Oil," with the statement that this monograph would become official on January 1, 1935. The only important change in the monograph for cod liver oil since that time is the change in minimum vitamin A potency from 600 to 850, which was prescribed in the Second Supplement to U. S. Pharmacopœia XI and which became effective on July 1, 1940. There have also been some minor revisions in the methods of assay.

The use of the U. S. Pharmacopœia Reference Cod Liver Oil as a standard for vitamin A and D assays has proven very satisfactory. Its present extensive use in the assay of cod liver oils for poultry feeding is largely responsible for the depletion of the supply of the first lot of oil. At the request of the International Vitamin Conference, this oil has been made available to foreign countries as a subsidiary standard for vitamin D. Active consideration of the preparation of a new lot of oil was initiated by the Vitamin Advisory Board more than two years ago, and a new lot has been acquired and bottled for distribution. Assays of the oil have been in progress during the past year.

Six years ago there was considerable interest in the adoption of a method for the determination of vitamin B_1 by the Pharmacopœia. The Federal Food and Drug Act of 1906 gave recognition to methods prescribed by the Pharmacopœia in the examination of products listed in that compendium, so that the desirability of such methods both from the standpoint of manufacturing control and for enforcement purposes is quite obvious. Three meetings of the U. S. P. Vitamin Committee have dealt largely with a method for determination of vitamin B. The first was held in New York in August, 1934; the second in Washington in March, 1936, and the third in New York in July, 1938. The extent to which interest has grown in the activities of this organization is evidenced by the fact that there were eighty-three persons present at the last meeting.

There was a wide divergence of opinion with respect to a suitable method at the first meeting. Preferences were expressed for a rat-growth method, a rat-curative method, a pigeon-weight-maintenance method, and a pigeon-curative method. The Vitamin Advisory Board

considered all of the proposals and recommended a collaborative study in which the relative value of these methods could be compared. The results of this study were considered at the next meeting and it appeared that any one of the four methods could be developed to a satisfactory degree of accuracy. The experience gained in this study was largely responsible for a preference for the rat-curative method. Of prime importance is the fact that it is specific, but it is also rapid, and the fact that it could be performed with that favorite of experimental animals, the rat, added to its popularity. Various modifications of the rat-curative procedure were proposed and the Vitamin Advisory Board decided to put these modifications to a crucial test before recommending an official method. Fourteen laboratories conducted assays of the same product using five prescribed modifications of the rat-curative procedure and the results were reported at the last meeting of the U. S. P. Vitamin Committee on July 8, 1938. On the basis of these results, the Board recommended the method of assay for vitamin B_1 which was included in the Second Supplement to U. S. P. XI, and which became official the first of this year.

I have attempted to cover very briefly the developments which have led to the present status of cod liver oil and the adoption of a method for vitamin B_1. I shall not attempt to review other activities of the board relating to Viosterol in Oil, Natural Vitamin A in Oil, Natural Vitamins A and D in Oil, Ascorbic Acid, Nicotinic Acid, and Thiamine Hydrochloride, which are now included in the Pharmacopœia. However, I do wish to bring to your attention the service the Pharmacopœia has rendered in providing vitamin standards.

While the League of Nations has provided this country with generous allotments of the international standards for vitamins A, B_1, C, and D, the demand for such standards for assay purposes greatly exceeds the quantities that we could hope to receive over an extended period. It has therefore been necessary to establish and distribute prototype standards that will serve the same purpose. I have already discussed the Reference Cod Liver Oil. The Board of Trustees of the Pharmacopœial Convention has also distributed a standard for vitamin B_1 similar in all respects to the standard adopted by the International Vitamin Conference in 1931. This standard was first issued in February, 1937. A little more than two years later this was replaced by crystalline vitamin B_1 hydrochloride which had then been adopted as the international standard. A crystalline vitamin C standard identical with the international standard is also issued by the Pharmacopœia.

These standards for vitamins A, B_1, C, and D are used in this country when vitamin potency is determined in U. S. P. units.

Different types of vitamin D do not produce the same biological response in different species. Rats cannot be used satisfactorily in determining the vitamin D potency of oil for poultry. The Association of Official Agricultural Chemists has prescribed a method for determining the vitamin D content of oils intended for poultry feeding in which chicks are used as the experimental animal. The U. S. P. Reference Cod Liver Oil is used as a standard in this method. This is cited as an example of the importance the Pharmacopœia has acquired in supplying vitamin standards.

A large part of the service that the Vitamin Advisory Board has rendered has been made possible by the very generous and helpful cooperation of those engaged in the manufacture of vitamin preparations who have conducted numerous vitamin assays and have taken a very active part in many phases of the work. No single factor has been more important in making for progress and directing the course to be followed than the meetings of the Vitamin Committee, which have permitted free and extensive discourse of all phases of our program. To all of those who have participated in this work the Vitamin Advisory Board is truly grateful.

OFFICIAL U. S. P. XI ARTICLES TO BE DELETED FROM U. S. P. XII

Acetum Scillae
Acidum Aceticum Dilutum
Acidum Acetyltannicum
Acidum Sulfuricum Aromaticum
Aconitum
Albumini Tannas
Ammonii Benzoas
Ammonii Bromidum
Ammonii Salicylas
Arseni Triiodidum
Asafoetida
Bismuthi Subgallas
Calcii Bromidum
Calcii Creosotas
Cannabis
Cantharis
Capsicum
Carbo Activatus
Carbromalum
Ceratum Cantharidis
Cinchona Colchici Semen
Copaiba
Creosoti Carbonas
Creosotum
Dichloramina-T
Emplastrum Cantharidis
Emulsum Asafoetidae
Extractum Cannabis
Extractum Nucis Vomicae
Ferrum
Fluidextractum Belladonnae Radicis
Fluidextractum Cannabis
Galla
Guaiacol
Hydrargyri Iodidum Flavum
Iodoformum
Kino
Liquor Ammonii Acetatis
Liquor Ferri Chloridi
Liquor Ferri Tersulfatis
Magma Ferri Hydroxidi
Massa Hydrargyri
Merbaphenum
Mistura Opii et Glycyrrhizae Composita
Oleum Santali
Pancreatinum
Paraffinum
Pepsinum
Pilocarpinae Nitras
Pilulae Aloes
Podophyllum
Potassii Chloras
Pulvis Ipecacuanhae et Opii
Pulvis Sennae Compositus
Pyrogallol
Quinina
Resina Podophylli
Santoninum
Scilla
Serpentaria
Sodii Acetas
Spiritus Aethylis Nitritis
Spiritus Chloroformi
Strychninae Nitras
Sulfonethylmethanum
Sulfur Lotum
Syrupus Ferri Iodidi
Syrupus Scillae
Terebenum
Theobromina cum Sodii Salicylate
Tincture Aconiti
Tinctura Cantharidis
Tinctura Capsici
Tinctura Cinchonae Compositа
Tinctura Colchici Seminis
Tinctura Ferri Chloridi
Tinctura Kino
Tinctura Scillae
Tinctura Valerianae
Tinctura Veratri Viridis
Unguentum Gallae
Valeriana Veratrum Viride

ABSTRACTS SELECTED

From Current Literature of the Sciences Supporting Public Health

Tannic Acid Scars. *Pharm. J., 91,* 169 (1940). Although tannic acid therapy has been hailed within recent years as a great advance over older methods in the treatment of burns it is not entirely without disadvantages. One of the lessons learned by those treating severe burns sustained by airmen is that in some regions of the body, at any rate, the scars cause such severe contraction of the tissues as to result in serious disability. This appears to be especially the case on the fingers and eyelids. Until quite recently first-aid workers were encouraged to apply some form of tannic acid preparation to burns of all types, and tannic acid jelly has found its way into the first aid equipment of many households. Now instructions have been revised and first aid posts, etc., have been told not to use tannic acid in the treatment of third-degree burns of the face and hands. In some hospitals washing the burned area with physiological saline or hypochlorite solution is on trial. A jelly containing 1 per cent. gentian violet and 1 in 5000 merthiolate in a water-soluble base has been recommended as a first aid dressing. The coagulum produced is more pliable than that which is formed by tannic acid and the solution has, of course, marked antiseptic value. In the prompt first aid treatment of burns, for example, caused at night by incendiary bombs it seems likely that after removal of burning clothing the application of one of the euflavine burn dressings is the best procedure to adopt. L. F. T.

Reduction of Arterial Blood Pressure of Hypertensive Patients and Animals with Extracts of Kidneys. I. H. Page, O. M. Helmer, K. G. Kohlstaedt, P. J. Fouts, and G. F. Kemph, *J. Exp. Med. 73,* 76 (1941). That the kidneys can not only initiate hypertension but also counteract it, is a fact which is suggested by an increasing amount of evidence. Rennin, which is present in the kidneys, and rennin activator interact to form a pressor substance called angiotonin, which raises the blood pressure by vasoconstriction. To oppose this action the kidneys also produce a substance which inhibits the vasopressor action of angiotonin and rennin. This inhibitor or

antipressor substance has been extracted by the authors from fresh pork kidneys, by several methods which they describe. A method for assaying these extracts is given which involves the development, and treatment, in dogs or rats, of experimental malignant hypertension. Tables and graphs are presented which show that in general the larger the dose the more prolonged is the reduction in arterial pressure, this time extending in some of the cases for several weeks with dogs. The value of one type of extract over any other was undecided.

The extract was administered to five human beings, with advanced malignant hypertension, with dramatic changes resulting. Headaches disappeared, dyspnea lessened, stupor banished, vision partially restored, and convulsions did not recur, when the blood pressure was reduced. An improvement of the state of the myocardium was also demonstrated. Graphs, charts, electrocardiographs, and case histories for these patients are presented. Other cases of essential hypertension yielded after treatment of a varying number of days. The authors feel that the active principle is slow acting and that a replenishment of depleted stores must first take place before treatment begins to be effective. The blood pressure is lowered in human beings with essential or malignant hypertension and in hypertensive dogs and rats for prolonged periods of time. The quantity of original fresh whole kidney required to yield enough extract to lower blood pressure from hypertensive levels to normal levels in dogs is roughly 600 to 900 grams within four to eight days. In hypertensive patients the yield from 700 to 1000 grams daily for several weeks may be necessary. The length of time the blood pressure remained lowered varies greatly in both man and animals. The trend is usually upwards after discontinuing treatment for four to six days. Increasing experience with this treatment suggests that it is of value in the management of hypertension, but it is yet in the experimental stage. W. T. F.

Nasal Filters for the Treatment of Common Colds. J. B. Biederman. *Clinical Medicine 47,* 418 (1940). The paper blames the "common cold" on a derangement of the vasomotor system, usually caused by a draft striking a part of the body which is normally not exposed to drafts. This is reflexly transmitted to the nasal membranes, impairing their normal functions, and permitting secondary infection with bacteria. The normal functions performed by the nasal

turbinates are the warming, moistening, and filtering of the air inhaled, and the secretion of a mildly antiseptic fluid.

Due to the disadvantages of the medicated steam inhalations which are as yet the most effective means of directly treating colds, the author advocates the use of a nasal filter, and describes a device which he has used.

The filter consists primarily of a replaceable and adjustable filter which can be inserted into the nostril and saturated with a few drops of a suitable volatile medicament. The filters act as substitute turbinates since they warm, filter, and moisten the air inhaled, and have a mild antiseptic action, and prevent cold air from striking the inflamed nasal membranes directly.

Of 200 patients treated in this manner, 68 per cent. were cured within twelve hours, and 94 per cent. within seventy-two hours, with no complications developing following the treatments. A further advantage of the filter, mentioned by the author, is that it permits free movement by the patient with no discomfort, during the treatment.

E. L. C.

Shark Livers as a Source of Vitamin A. *Drug and Cosmetic Industry 47*, 537 (1940). Because of war conditions the cod liver oil supplies in this country may become acute since not more than 5 per cent. of domestic consumption is produced right here in the United States. The future source of vitamin oils will have to be from fish other than cod, and it seems that our domestic waters yield fish in large enough quantities to make them commercially important as sources of oil rich in vitamins A and D.

Shark fishing offers probably the greatest possibilities as a source of vitamin A because, first, there are about ten different varieties of shark which can be caught off the coast of Florida alone. Secondly, the ratio of liver to body weight is roughly 8-12 per cent. and has been reported as high as 30 per cent.; and the oil content of the livers is between 30 and 70 per cent. Thus, where cod liver oil is obtained by the ounce, shark liver oil may be had by the gallon. Thirdly, sharks are valuable not only for their liver oil but like the hog of packing house fame, may be almost entirely utilized. It is not surprising, therefore, that the shark is being used, especially on the West coast, as a profitable field of exploitation. This can be substantiated by the following figures. In 1930 total landings of shark in California

amounted to 647,297 pounds, while in 1939 it amounted to 9,156,572 pounds. Just what the future holds for the industry is unpredictable.

Methods used for the extraction of liver oils vary from heating the minced livers in open tubs and skimming the oil off the surface, to highly refined methods where everything is under laboratory control.

One fact must be kept in mind with reference to shark liver oil, namely, that it is rather low in vitamin D; the ratio being 300 units of A to a single unit of vitamin A. However, shark oil can be easily fortified with oils from fish yielded by our domestic waters, particularly sardine, which has a good percentage of vitamin D.

Without a doubt, the possibilities of shark liver oil as a permanent and important source of vitamins is very great and merely needs more investigation. E. A. M.

Aluminum Hydroxide as an Emulsifying Agent. S. J. Hopkins. *Aust. J. Pharm. 21,* 798 (1940). Aluminum hydroxide, which is prepared from a soluble aluminium salt and sodium carbonate, is described. The precipitated hydroxide is washed free from soluble salts, suspended in water, and then "ripened," either by exposure to ultra-violet light or bright sunshine, or by boiling the suspension. The suspension of activated alumina then has the excess of water removed by means of a filter-press. The finished product is a stiff paste, containing approximately 10 per cent. of alumina.

Emulsions can be made by diluting the agent with the aqueous phase, either by trituration or agitation, and then adding the disperse phase, the mixture being passed through homogenizer. Oleic acid in a very small amount if added will give a better emulsion in cases where a high proportion of oil is to be incorporated.

The proportions for using this new agent are variable, but as a general rule from 2 to 10 per cent. of the agent, based on the total volume of finished emulsion, should be used.

This new agent may also be used as suspending agent, and as a wetting agent for water-repelling substances such as precipitated sulfur. It possesses all the significant properties of an emulsifier, including suitability for internal use. C. S.

The Detection and Estimation of Benzedrine. E. T. Illing. *Analyst 65,* 3 (1940). Benzedrine or B-Aminopropylbenzene ($C_9H_{13}N$) is chemically allied to ephedrine and adrenaline. It is a liquid, slightly soluble in water, more soluble in alcohol and readily

soluble in acids, ether, amyl alcohol, ethyl acetate and chloroform. It is completely volatile at 100 degrees C.

Estimation for Benzedrine in Aqueous Solutions. Benzedrine is extracted from an alkaline solution by means of chloroform. The benzedrine is then re-extracted from the chloroform by shaking out with $N/_2HCl$. The acid extracts are evaporated to dryness, the residue is dissolved in absolute alcohol, filtered and again evaporated to dryness. The calculation is then based upon the amount of benzedrine obtained.

Test for Benzedrine. A new test has been found very effective in the detection of the Hydrochloride. It consists of a modification of the Mohler Test. (E. T. Illing, *Analyst,* 1932, *57,* 225). This test consists essentially of the production of a purple color which is compared colorimetrically with a standard. This test is capable of detecting 0.1 mg. of Benzedrine HCl.

Detection of Benzedrine by Distillation. The Benzedrine salt is placed in an alkaline solution and steam distilled. The distillate is passed through 2 portions of $N/_1HCl$ contained in separate flasks. The combined filtrates after being evaporated, to a small volume, are made alkaline and then extracted as described above.

Extraction of Benzedrine from Viscera. This is accomplished by the Stas-Otto process. The Benzedrine is extracted from the alkaline solution with chloroform.

Extraction from Urine. The Benzedrine urine mixture is steam distilled for one hour. The distillate is then subjected to Mohler's Test.

Benzedrine Tablets. A portion of crushed tablets is treated with solid $BaCl_2$ and $N/_1HCl$. Alcohol is added. The mixture is then filtered. The alcohol is then evaporated off. The liquid is then filtered into a separator. An excess of alkali is added to the filtrate. The extractions are then made with chloroform.

Distillation of Tablets of the HCl. The salt is distilled from an alkaline solution for one hour. The recovered Benzedrine is then treated as described above.

Tablets of the sulfate may be determined gravimetrically as follows: HCl is added to the tablets, a barium salt is added. The ppt of $BaSo_4$ is then collected and weighed. H. R.

Use of Miniature X-Ray Films in Tuberculosis Case Findings. B. H. Douglas, C. C. Birkelo, G. E. Harmon and H. F.

Vaughan. *Amer. J. Pub. Health 30,* 1427 (1940). With the sources of bovine infection cut to a small fraction of their previous importance, the human cases remain the chief sources of infection with the tubercle bacillus. Since the average patient does not present himself for examination until he is seriously ill and, therefore, beyond the point of most useful treatment, it is necessary that a method be adopted whereby cases may be found early. A study was conducted in Detroit among three groups previously noted to have a higher than average prevalence of tuberculosis, namely: contacts with known cases, suspects with symptoms and those residing in areas with high tuberculosis mortality. During the three and one-half years' operation of this study, 136,812 persons were tuberculin tested and 38,395 reactors, or 29 per cent, were found; 34,059 of the reactors were examined by X-ray and 890 new cases requiring treatment were detected. Because of the necessity of a visit for testing, a revisit for reading and another visit for the X-ray, many examinations were not completed.

Since the X-ray examination of the chest is the best means of detecting early pulmonary tuberculosis, it is desirable to have an inexpensive but accurate method for making such examinations so that it may be used as a single procedure, thus avoiding losses due to inaccuracies of a single dose tuberculin test, failure to have the test read or failure to go for an X-ray examination when the test is found positive. A technique has been developed utilizing a 4 x 5-inch fluorograph. The method has been checked for accuracy when compared with a full size film and has shown negligible error. A proof of the value of the technique came when 1425 women coming to the pre-natal clinic of the Department of Health were tuberculin tested with a single dose of 1/1000 O. T. and X-rayed. Of the 144 who failed to return for the reading, 2 were shown by the X-ray to be active pulmonary cases. Of the 1281 who returned for a reading, 610 were positive. Among the positive were 3 active cases. Among the 671 negatives there were 2 active cases found by X-ray. Hence, a single visit for an X-ray examination eliminates the possibility of missed cases.

In conclusion, the studies indicate that the 4 x 5-inch fluorograph is: (1) accurate in comparison with large standard films, (2) useful without previous tuberculin screening, (3) economical and can be applied rapidly to large numbers for survey purposes, and (4) favorably comparable with other methods of X-ray examination which have been applied to large numbers. E. E. L.

Effect of Alcohol on Vitamin A Content of Blood in Human Subjects. S. W. Clausen, B. B. Brese, W. S. Baum, A. B. McCoord and J. O. Rydeen. *Science 93,* 21 (1941). Observations were made on the vitamin A content of the blood in humans before and after taking alcohol. The Carr-Price colorimetric method, modified by Clausen, was used for the determination. The alcohol was taken in the course of an evening of "social" drinking. In every case, as shown in the table below, there was some increase in the vitamin A content of the blood after taking alcohol. Subject B showed a remarkably high content initially and a superior rise after ingestion of alcohol. No vitamin A concentrates had been taken previously.

					Evelyn photoelectric units of vitamin A per 100 ml of serum*		
Subject	Age	Sex	Weight lbs.	Amount of alcohol (95%)	Basal	Four hours after alcohol	Twelve hours after alcohol
A	35	M	170	135 cc	33.8	42.1	42.9
A				145 cc	47.6	50.0	46.6
B	30	M	160	162 cc	93.4	217.7	76.5
C	35	M	160	150 cc	30.5	45.3	41.7
D	31	M	170	126 cc	50.8	54.3	48.3
E	36	F	120	54 cc	40.5	42.2	40.7
F	30	M	240	216 cc	57.0	59.8	48.2
G	29	F	150	261 cc	48.4	60.1	39.5
						Two hours	
H	35	M	160	20 cc	37.8	38.7	
I	33	M	150	20 cc	60.3	62.2	

*One Evelyn photoelectric unit of vitamin A is approximately equal to three international units of vitamin A.

The authors suggest that the rise of vitamin content in the blood is due to a shift of the vitamin from other tissues of the body. The amount of alcohol ingested, the saturation of the body with vitamin A and the tolerance to alcohol may be factors influencing the rise.

E. E. L.

Ergot and Ergonovine. Gordon A. Bergy and Marvin R. Thompson. *American Professional Pharmacist 6,* 782 (1940). This new water-soluble alkaloid of ergot, apparently much less toxic than ergotamine and ergotoxine, promises to be a major advance in present and future therapy involving uterine action. J. E. K.

The Excretion of Specific Fluorescent Substances in the Urine in Pellagra. V. A. Najjar and L. E. Holt, Jr. *Science 93,* 20 (1941). When urine is adsorbed on zeolite and eluted with KCl, the eluate on treatment with NaOH develops a bluish fluorescence, apparently dependent upon the store of nicotinic acid in the body, as described in a previous paper (Najjar and Wood, *Proc. Soc. Exp. Biol. & Med. 44,* 386 (1940). A fluorophotometer was used to measure quantitatively the fluorescence.

A study has now been made of four patients with typical pellagra, one of mild intensity, two moderate and one unusually severe. The urine of none of these patients showed the characteristic fluorescence when treated as previously described. However, this urine when not treated with alkali showed the presence of four to five times the amount of the whitish-blue fluorescence found in normal urine. Hence, two fluorescent substances may be said to be influenced by the nicotinic acid content of the body, one, measurable in urine without alkali treatment and increasing with deficiency of nicotinic acid, is designated as F_1; the other, measurable in urine eluates after alkali addition and decreasing with deficiency of nicotinic acid, F_2.

The earliest change in pellagra is the disappearance of F_2. As the disease progresses the increase in F_1 becomes more and more striking. Conversely, with treatment F_1 first decreases and subsequently F_2 appears.

The authors interpret their results as indicating the presence of an enzyme of which nicotinic acid is a component. Normally this enzyme converts F_1 into F_2. In states of nicotinic acid deficiency this conversion cannot take place and F_1 accumulates.

E. E. L.

Alkyl Ethers, 2, 4-Dinitrophenol as Stimulants of the Metabolic Rate. L. G. Wesson. *J. Am. Chem. Soc. 62,* 3466 (1940). Fatalities in cases of dinitrophenol poisoning result from a rapid hyperthermia. In the attempt to develop derivatives of dinitrophenol that would have a more gradual and moderate action on the body metabolism, there was prepared a series of alkyl ethers of dinitrophenol. The isopropyl analog appeared most promising, having a low degree of toxicity and a protracted increase of the metabolic rate,

together with a favorable melting point and ease and cheapness of preparation. Its method of preparation consists in reacting the corresponding alcohol (isopropyl) with dinitrochlorobenzene in presence of an alkali (KOH). Procedures of previous workers gave a product having a high content of the toxic dinitrochlorobenzene, and hence unsuitable pharmacologically. Wesson's method is a modification to obviate this difficulty. Also made were the n-propyl, n- and isobutyl, n- and isoamyl, n-hexyl and n-heptyl compounds, using a different method, viz., reacting Ag dinitrophenol with the corresponding alkyl halide. The more gradual effect of these ethers as compared with dinitrophenol itself in stimulating the metabolic rate of rats is shown. The isopropyl ether showed the most gradual metabolic increase per hour, as well as the smallest amount ammonia excreted, the latter presumably from liver damage. Twelve rats fed a diet of fox chow containing 0.1 per cent. of the isopropyl ether for eight months evidenced no discernible effect. Except for a smaller amount of fat than in the six controls, no other difference was found on necropsy of the rats. Effect of massive doses (1 g. per kg. of body weight) was to markedly raise the metabolic rate (84 per cent. over the basal) and to produce death of the rats in the characteristic dinitrophenol rigor. The author raises the question as to whether the pharmacologic action was due to the ethers themselves or to free dinitrophenol formed by hydrolysis.

W. S.

The Preparation and Study of Silver Antiseptics with and without Ephedrine. A. Slesser and C. B. Jordan. *Jour. A. Ph. A. 22,* 514 (1940). The therapeutic effect of silver in protein combinations brings it into much use in eye, nose and urinary tract infections. Various emulsions of silver with and without ephedrine have been prepared and found to have reasonably good zones of penetration. Three new soluble silver salts having antiseptic properties have been prepared. The stability of ephedrine-silver mixtures may be enhanced by the additions of such substances as gelatin, acacia, sucrose and urea. Addition of reducing substances is unsatisfactory.

J. E. K.

S O L I D

EXTRACTS

Prepared for the readers of the American Journal of Pharmacy by the Editor and his staff

Following through last month's editorial on the possibility of America's self-sufficiency in vital crude drugs, it is interesting to note that more than 250 drug plants are normally collected in the United States. These plants are, for the most part, quite ready to respond to the climate of the particular parts of the country in which they have been collected commercially for many years, and do not require any coddling or coaxing beyond that given any crop which the grower hopes to be successful.

Who knows but what there may be many other plants abounding close by, totally ignored by our pharmacognosists and pharmacologists, budding and blooming time and time again, just ripe to replace some European drug plants now denied us because of the tumult and the shooting abroad. It is indeed a challenge to our resourcefulness.

Experiences in World War I indicate that many immigrant drugs can be cultivated here when freight-loaded boats no longer pass the Statue of Liberty coming our way. But as soon as these conditions are reversed, foreign labor and native cultivation can ruin the American industry, thus making us undesirous of starting the project in the first place. Right now, the seriousness of the situation demands prompt propagation, cultivation, investigation and domestication to achieve a declaration of independence from European sources.

Officials of the U. S. P. are seriously considering the adoption of various procurable oils to substitute for oils of rose and lavender in official preparations, the latter being so scarce and so important because they are included in several official formulas.

Not only are some drugs becoming scarce in this country, but likewise properly trained druggists. At a recent quarterly examination conducted by the State Board of the great Commonwealth of Pennsylvania, only four applicants presented themselves.

No longer has youth, or any of youth's advisers, any justification in saying that there are no opporunities in the profession of pharmacy.

That troublesome pipe line may be suffering from "bacteriosis," to coin a term in want of a better one. According to a pipe line engineer, untold damage has been done to underground water, gas and oil lines of iron and steel by an anærobic type of bacteria, very hardy and resistant to extremes in temperature.

Just as sulfathiazole is being acclaimed for its marvelous properties of battling bacteria in the human body, penicillin, from penicillium, one of the blue-green mold group, is found experimentally to have several times the bactericidal action of the current chemotherapeutic hero of the sulfonamide group. Further tests are being made. Science marches on.

Despite this progress, it is somewhat discouraging to note that the "sulfa" family's one demerit in the public eye, the elixir incident, is still being talked about in the press. As late as November, 1940, the story of the unfortunate happening was the opening topic of an article on sulfanilamide in a more or less popular science magazine.

The "flu" epidemic which is sweeping from Honolulu through the United States and is said to be heading for Europe, even though mild, will afford plenty of opportunity for clinical proof of the efficacy of the "sulfa" group, and many citizens of many lands will witness future events in this uncertain world through the courtesy, may we say, of one of these chemotherapeutic agents.

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